Thalassemia in a Hawaiian Family of Filipino Extraction

By Harold P. Lazar

Interest has been focused recently upon the hemoglobinopathies and their elucidation by means of electrophoresis. Included among these are thalassemia, sickle cell anemia, hemoglobin C, D, and E disease, and their combinations, all of which share in common a number of hematologic abnormalities. Dameshek has stated that the diagnosis of thalassemia is made from a number of more or less nonspecific hematologic findings in the absence of a demonstrable electrophoretic abnormality of hemoglobin. For example, the study of thalassemia in Thailand has been reinterpreted as representing a combination of thalassemia and Hgb E disease. It is the purpose of this paper to present a study of thalassemia in a Hawaiian family of Filipino extraction, with a complete study of the case which prompted the investigation.

Case Report

Alberto E. is a 19 year old Air Force basic trainee born in Hawaii of Filipino parents; one of 12 siblings. He was admitted to the 3275th USAF Hospital at Parks Air Force Base, California, on June 24, 1955, with typical rubella. Past history and family history were not contributory. Physical examination, apart from the manifestations of rubella, was not remarkable except for a firm spleen tip palpable 4 cm. below the left costal margin. Initial hemogram revealed a hemoglobin of 9.6 grams per 100 cc. with a hematocrit of 39 per cent. Hemoglobin levels ranged from 9.2 to 11.5 grams per 100 cc., and erythrocyte counts were between 5.1 and 7.58 million per cu.mm. during the study period. Peripheral blood smear revealed hypochromia, anisocytosis, poikilocytosis, polychromatophilia, ovalocytosis, and target cells. Platelet counts and reticulocyte counts were not remarkable except for isolated reticulocyte counts of 2.0 and 2.6 per cent.

Admission urinalysis revealed a trace of albumin which rapidly cleared. Throat culture revealed alpha and beta hemolytic streptococci. Blood urea nitrogen was 15 mg. per 100 cc. Liver function tests, including total protein, albumin, globulin, bilirubin, cholesterol and esters, prothrombin time, bromsulfalein retention, thymol turbidity, cephalin flocculation, and alkaline phosphatase, were all within normal limits. Sternal marrow examination revealed a hyperplastic marrow. Rumpel-Leede test, clot retraction, bleeding time, and coagulation time were normal. Urine urobilinogen was within normal limits. A chest film was negative, as were skull films and a bone series. On the initial cholecystogram, with poor visualization, one small calcific density was identified in the fundus in three projections. A repeat examination one month later revealed better visualization, but the calculus could not be demonstrated at that time. The alkali-resistant hemoglobin, according to the method of Singer, was within normal limits, and, on paper electrophoresis, only one component having the mobility of hemoglobin A was found. These latter two studies were repeated and confirmed in the laboratories of Dr. John H. Lawrence and Dr. Karl.

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I wish to thank Dr. John H. Lawrence and Dr. Myron Pollycove of the Donner Laboratory and the late Dr. Karl Singer of Michael Reese Hospital for their interest in aiding this study. I also wish to acknowledge the assistance of Lt. Col. Harold E. Shuey, M.C., USA, and the laboratory staff at Tripler Army Hospital as well as Mr. Donald Lamanna and S/Sgt. Charles W. Striker of the laboratory staff of the 3275th USAF Hospital for their special efforts in this investigation.

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Singer. A Tiselius study performed in Dr. Singer's laboratory revealed only hemoglobin A. Osmotic fragility was decreased beginning at 0.40 per cent saline and incomplete at 0.20 per cent. Several sickling preparations employing the sodium metabisulfite method were normal. Radioactive iron turnover studies were performed at the Donner Laboratory through the kindness of Dr. John H. Lawrence and Dr. Myron Pollycove. Since it is not especially germane to the present family study, suffice it to say that the isotope investigation was interpreted as revealing a moderate degree of random destruction of erythrocytes in the spleen only partially compensated for by increased marrow erythropoiesis. A detailed account of the iron metabolism study will be found in a report to be published by the group at the Donner Laboratory.

Upon completion of these studies, since no therapy was indicated, the patient was returned to duty with no limitation or restrictions, completely asymptomatic.

**Family Study**

Through the kind cooperation of Lt. Col. Harold E. Shuey, Chief of the Laboratory Service at the Tripler Army Hospital in Hawaii, we were able to contact and study the family of Alberto E. The best information we could obtain was that the parents, Ariston

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**Figure 1:** Pedigree of Family E. Thalassemia trait represented by cross-hatching.

**Table 1: Hematologic & Clinical Data on the E. Family**

<table>
<thead>
<tr>
<th>NAME</th>
<th>AGE</th>
<th>Hb (g/dl)</th>
<th>Hct</th>
<th>RBC (mill)</th>
<th>MCV</th>
<th>MCH</th>
<th>MCHC</th>
<th>Retic. count</th>
<th>Erythropoiesis</th>
<th>Leukocytes</th>
<th>X-RAYS</th>
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<td>Ernest</td>
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<td>40</td>
<td>4.88</td>
<td>5.03</td>
<td>3.8</td>
<td>37</td>
<td>4+</td>
<td>1+</td>
<td>0.8</td>
<td>++</td>
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<td>40</td>
<td>6.65</td>
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<td>3.8</td>
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<td>++</td>
</tr>
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<td>40</td>
<td>6.65</td>
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<td>3.8</td>
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<td>37</td>
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<tr>
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<td>40</td>
<td>6.65</td>
<td>5.03</td>
<td>3.8</td>
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<td>6.65</td>
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<td>3.8</td>
<td>37</td>
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<td>1+</td>
<td>0.8</td>
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<tr>
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<td>3.8</td>
<td>37</td>
<td>4+</td>
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<td>0.8</td>
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<tr>
<td>Frances</td>
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<td>0.8</td>
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and Tiborcia E., had been born in the Philippine Islands, whence they emigrated to the Hawaiian Islands, where all the offspring were born. Our only information concerning the family is hematologic and roentgenographic, since these individuals did not undergo physical examinations. To the best of our knowledge they were all asymptomatic. One daughter, Nancy E. B., living in Los Angeles, was not studied. Only Alberto E. had an alkali-resistant hemoglobin determination and hemoglobin electrophoresis. The data are summarized in Table 1. A distinct tendency exists for decreased osmotic fragility. The affected members, Ariston E., Alberto E., Alfred E., Mercy E. P., Martha E., and Beatrice E., all exhibited an erythrocytosis of 5.5 million per cu. mm. or more, and depression of the MCV and MCH were found, in the presence of an only slightly reduced MCHC. Erythrocyte morphology, as determined by examination of the peripheral blood smear, was appropriate. None of the bone roentgenograms demonstrated abnormalities. It is of interest to note that the MCHC recorded for Alberto E. in Table 1 is 28.2 per cent, representing the highest value obtained. On numerous other examinations the values tended to run lower, even to 23 and 24 per cent. Characteristically one would have expected a decreased MCH and MCV in the presence of a normal or only very slightly decreased MCHC. We attributed this discrepancy to an inability to determine a true hematocrit, perhaps inherent in our centrifugation, since our photoelectric hemoglobinometry has been accurate.

**Discussion**

A brief consideration of the ethnic group under scrutiny seems appropriate. The inhabitants of the Hawaiian Islands comprise a heterogeneous group, with their background of intermarriage. The 1950 census sets the total population at 493,437 with the following racial backgrounds: Japanese 36.7 per cent; Caucasian 22.8 per cent; pure Hawaiian and part Hawaiian 17.5 per cent; Filipino 12 per cent; Chinese 6.7 per cent; and other, including Puerto Rican, 4.3 per cent. The Family E., however, is readily traceable to the Philippine Islands, and no apparent mixture has occurred.

Perhaps the best scheme for classification has been proposed by Singer et al., who divide thalassemia into five groups: Thalassemia major, thalassemia intermedia (less severe, but marked anemia), thalassemia minor (mild anemia), microcytic erythrocytosis, and thalassemia minima (slight leucoerytosis only). Alberto and Beatrice represent examples of Thalassemia minor, while the other affected members would fall into one of the latter two categories. Thalassemia minor may or may not be associated with an elevation of alkali-resistant hemoglobin, and only in the case of Alberto was this investigated. Assuming the father, Ariston E., to be heterozygous for the thalassemia factor, five of twelve studied offspring demonstrated distinct evidence of the trait, approximately what one would expect through chance distribution, assuming transmission through a Mendelian dominant mechanism, though previous investigations had held it to be otherwise. Chernoff has suggested that the clinical manifestations are better explained by multiple interrelated genetic defects rather than by a single set of alleles.

Of some concern is the fact that hemoglobin electrophoresis was not performed on the entire family. A recent report by Schwartz has emphasized the role of electrophoresis in distinguishing between hemoglobin C disease and thalassemia. This review and reappraisal of previously published cases suggests that perhaps others which were represented in the past as thalassemia may indeed have been instances of specific hemoglobinopathy, since most of these were reported before the era of paper electrophoresis.
Numerous previous reports, prior to electrophoretic studies, have expanded the earlier concepts of the distribution of thalassemia, previously thought to be limited to Italians, Greeks, Cypriots, and other Mediterranean peoples. The initial recognition of a less severe form of “Cooley’s anemia” was made by three groups working independently. These workers studied the incidence of thalassemia in the Italian population of Rochester, New York, and found thalassemia major to occur in the ratio of 1 in 2308, while thalassemia minor occurred in 1 in 25.

Well documented reports, most without electrophoretic studies, have implicated Chinese, Indians, Egyptians, Negroes, Jews from Kurdistan, Filipinos, and a Scottish family. Changing concepts regarding the significance and distribution of thalassemia seem to have all but erased the previously supposed ethnic specificity. Continuing research into the mechanism and dynamics of the condition may elucidate some heretofore unrecognized molecular hemoglobin alteration. At present it is probably best to tread carefully in differentiating it from the now specifically regarded hemoglobinopathies so easily demonstrable on paper electrophoresis.

SUMMARY

Hematologic data are presented on thalassemia in a Hawaiian family of Filipino extraction, and support is given the recent trend to broaden the ethnic concept of thalassemia. Because of recent reappraisals of older reported cases by other investigators in the light of newer electrophoretic techniques, the need for continued re-evaluation is suggested.

SUMMARIO IN INTERLINGUA

Es presentate datos hematologic super le thalassemia un familia hawaiian de extraction philippin. Le datos appoia le recente tendentia a allargar le concepto del distribution ethnic de thalassemia. Viste le recente reevalutatione, in le lumine de nove tecnicas electrophoretic, de casos previemente reportate per altere investigatores, nos suggere le necessitate del continue reevalutation del datos.

REFERENCES


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